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### Developments in diagnosis and treatment of obstructive sleep apnea

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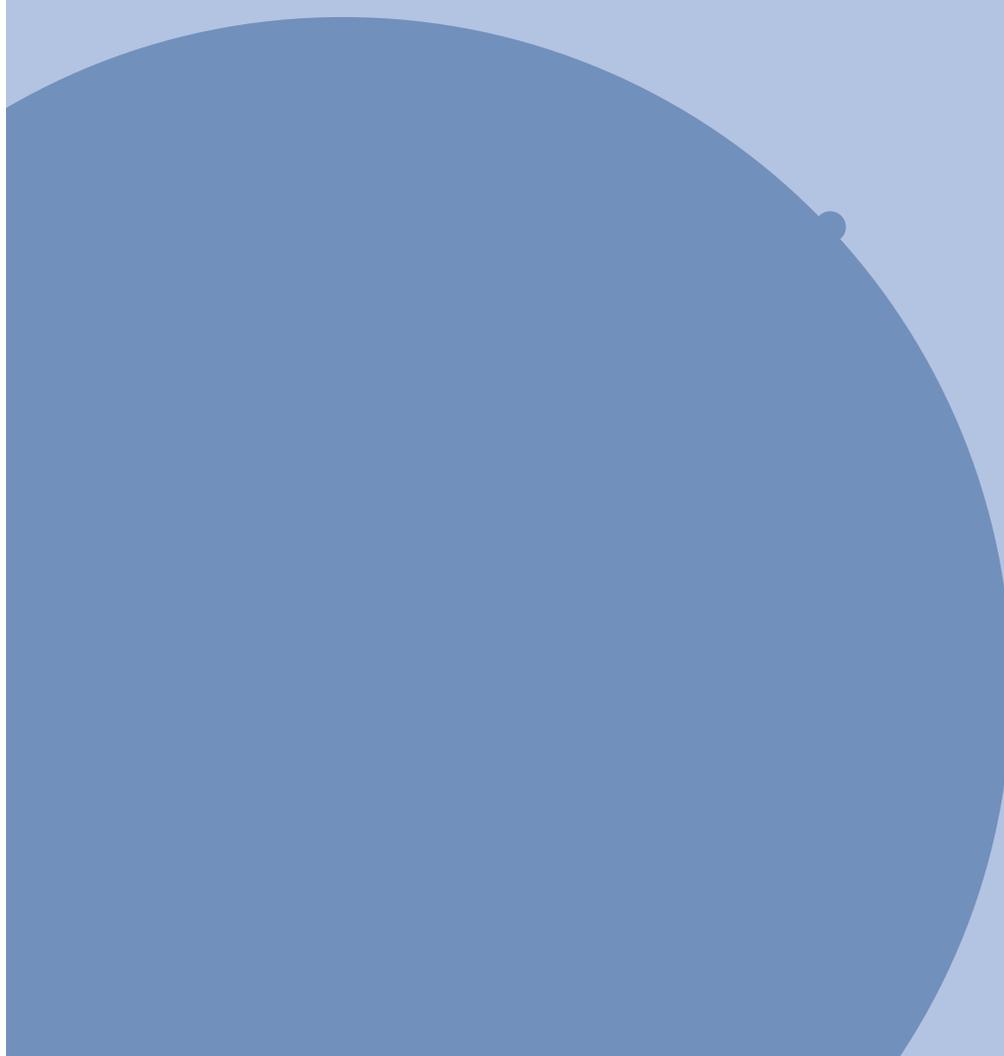
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# 9 Daytime polysomnography to perform titration for upper airway stimulation in patients with obstructive sleep apnea.

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## ABSTRACT

**Purpose:** Upper airway stimulation (UAS) is an innovative treatment for patients with obstructive sleep apnea (OSA). UAS titrations are performed 3 months after activation of the device to optimize its effectiveness. In general, these titrations are performed during an in-laboratory overnight polysomnography (PSG). However overnight titrations are expensive and can be logistically challenging because it's labor-intensive which causes shortage of sleep technicians available for night shifts. In addition, recently, overnight PSGs were postponed and cancelled due to the COVID-19 pandemic. We aimed to research the feasibility of a daytime PSG to perform titration of UAS therapy as an alternative for a conventional overnight PSG.

**Methods:** Prospective single-center observational cohort study. Patients were included when planned for UAS titration, this was approximately six months after UAS activation. Data on sleep architecture, patient experience and respiratory outcomes were collected to evaluate the feasibility. An overnight follow-up PSG 12 months after implantation was used to compare sleep architecture and therapy response.

**Results:** Twenty-three patients were included, four were excluded for analysis because of technical issues during PSG. Even though patients slept significantly shorter during the daytime PSG, this was enough time to complete the titration successfully with 30 minutes sleep in final therapeutic settings in 84.2% of the patients. Patients (94.1%) had a positive experience with the daytime titration. Respiratory outcomes were significantly reduced during titration and were maintained at the 12-months follow-up.

**Conclusion:** Daytime titrations are a valuable alternative for conventional overnight titrations. Our findings suggest the implementation of daytime titrations as standard of care. This will contribute to easier logistics and better work circumstances for sleep technicians without jeopardizing titration quality.

**Keywords:** Upper airway stimulation; daytime polysomnography; device titration; obstructive sleep apnea; sleep medicine

## INTRODUCTION

Continuous positive airway pressure (CPAP) is the gold standard therapy for patients with moderate to severe obstructive sleep apnea (OSA), proven to be highly effective in reducing complaints and comorbidities. [1-3] Despite its high efficacy, many patients are unable to tolerate treatment with CPAP.

An alternative treatment for a specific group of patients is hypoglossal nerve stimulation (HNS; Inspire® Medical Systems, Inc.), also referred to as upper airway stimulation (UAS). The protrusion fibers of the hypoglossal are stimulated by using unilateral stimulation, mainly innervating tongue protrusion. The neurostimulator delivers electrical stimulating pulses to the hypoglossal nerve through the stimulation lead; the stimulating pulses are synchronized with ventilation detected by the sensing lead. This ensures the patency of the upper airway. UAS therapy has demonstrated a significant improvement in OSA outcomes, good therapy adherence and high patient satisfaction. [4, 5]

Patients are eligible for UAS device implantation when strict selection criteria are met. [6] In general, four to six weeks after implantation the UAS device is activated with standard settings. The device will be slowly up-titrated at home until patient's symptoms such as decreased sleep quality, daytime sleepiness and snoring have improved. An in-lab overnight titration polysomnography (PSG) is subsequently performed once patients are accustomed to the stimulation and subjective symptoms have improved. The main purpose of the titration is to establish a comfortable but effective device setting to maintain upper airway patency during sleep. This titration is performed by a trained sleep technician. During this titration the UAS device settings are optimized and titrated until respiratory events are normalized. Electrode configuration, stimulation amplitude and stimulation pulse width and rate can be adjusted. The final settings should minimize the occurrence of obstructive events and should not cause arousals. [7]

Traditionally titrations were performed in-lab and overnight which is logistically challenging and expensive. They are mainly labor-intensive because sleep technicians have to be available during the night. Another havoc presented itself during the COVID-19 pandemic. Sleep laboratories were often imposed to resign overnight hospital beds due to shortages. As a result, overnight sleep studies were often postponed resulting in long waiting lists. Also, the growing amount of patients with UAS device asks for a more accessible way to perform titrations.

An alternative for an overnight titration is a daytime titration. Several studies have investigated the role of a daytime PSG in diagnosing OSA, concluding that a daytime PSG is a viable and effective alternative [8-10]. Other studies have investigated the role of a daytime PSG in CPAP titrations, concluding that a daytime PSG is a useful tool for CPAP titration [11-14]. To date, the role of a daytime PSG in UAS titration has not yet been investigated.

A daytime PSG might be a valuable alternative for an overnight PSG to perform titration in the context of UAS optimization. The benefit of a daytime PSG for titration is that sleep technicians do not have to work during the night and sleep studies will not have to be postponed due to bed and staff shortage. The aim of this study is to assess the feasibility of a daytime PSG to perform titration of UAS therapy in patients with OSA. Effect on sleep architecture, titration success and practicality and patients experience with daytime titration was evaluated. Secondary, respiratory outcomes from UAS therapy during titration were evaluated and compared to the outcomes after 12 months of therapy use.

## **MATERIAL AND METHODS**

### **Study participants**

We performed a prospective single-center observational cohort study including OSA patients with UAS therapy. Yearly about 35 patients with severe OSA receive UAS implantation at the department of Otorhinolaryngology/Head and Neck Surgery in OLVG hospital, Amsterdam, the Netherlands. [15] Patients were included from September 2019 to January 2021 if they were scheduled for a standard in-lab PSG for titration which was approximately 3 months after device activation. They were included if they were 18 years or older and were able to speak, read and write in Dutch. Instead of the standard overnight in-lab PSG, a daytime in-lab PSG was used to perform titration.

Patients were admitted the night prior to their daytime titration PSG and were instructed not to sleep. The following morning the patients were asked to document caffeine, nicotine or alcohol consumption during the night. Other questions included their experience with UAS and sleep quality during the past months at home. The UAS device system was checked and subsequently all components were applied to

perform the PSG. At 08:00 a.m. patients were asked to go to sleep. Patients slept in a soundproof room with no daylight. The PSG was observed by a sleep technician, who at the same time performed the titration. The sleep technician checked if all sleep stages were reached while the optimization process took place.

Sleep architecture data from the daytime titration was compared to the 12 months PSG (which is standard of care) after implantation. The latter was either performed at home or in-lab with the device switched on.

Effectiveness of UAS was investigated comparing respiratory outcomes between the pre-operative PSG and the 12 months PSG, as described above. The therapeutic AHI achieved during the daytime titration was also compared to the AHI measured during the 12 months follow-up PSG.

Patient experience with the daytime titration was asked during a follow-up appointment a week after titration.

## **Ethical considerations**

This study was conducted with approval of the local advisory committee for scientific research of the OLVG hospital, Amsterdam, the Netherlands. To protect personal information all data on participants was collected and stored encoded. All participants signed informed consent.

## **Polysomnography**

A standard polysomnography (Somnoscreen™, SOMNOmedics GmbH, Randersacker, Germany) was performed in all patients. To determine the stages of sleep, an electroencephalogram (F3, F4, C3, C4, M1, M2, O1, O2), electro-oculogram and electromyogram of the submental muscle were obtained. Nasal airflow was measured by a nasal cannula/ pressure transducer inserted in the opening of the nostrils. An oronasal thermal flow sensor was used to determine the difference between the temperature of exhaled and ambient air to estimate airflow and detect mouth breathing. Arterial blood oxyhemoglobin was recorded with the use of a finger pulse oximeter. Thoracoabdominal excursions were measured qualitatively by respiratory effort belts placed over the rib cage and abdomen. Body position was determined by a position sensor, which differentiates between the upright, left side, right side, prone and supine position. Limb movements were detected with

an anterior tibial electromyogram with surface electrodes. Electrocardiography was performed to score cardiac events and snore sensor was applied for occurrence of snoring.

## Scoring

The sleep stages were scored manually by an experienced sleep investigator in 30-s epochs according to the American Academy of Sleep Medicine (AASM, scoring manual version 2.6, 2020) scoring manual, with N3 representing slow wave sleep. Both daytime PSG and follow-up PSG were scored by the same sleep technician and neurosomnologist, the scoring was not blinded.

## Titration

The main purpose of titration was to optimize the UAS device settings until respiratory events were eliminated or reduced to a clinically satisfactory level. The sleep technician paid attention to several titration parameters such as amplitude, polarity and stimulation duration. The sleep technician started the UAS therapy once the patient was in consolidated sleep and the individual start delay of the UAS device had expired. The stimulation level started with 0.2V amplitude below the functional threshold and was therefore unlikely to provoke an arousal. The stimulation setting was increased with 0.1V or 0.2V amplitude when four or more serial obstructive events or loud ambiguous snoring occurred. The patient was observed in all non-rapid eye movement (NREM) sleep stages and REM sleep, preferably containing REM sleep in supine position, for optimal titration settings. The titration was finished when the patient had slept for 30 minutes straight with the final settings, ideally with an apnea-hypopnea index (AHI) < 5. Preferably these 30 minutes contained rapid eye movement (REM) sleep and sleep in supine position. When this was not achieved the sleep technician ended the titration when the patient had slept through at least 2 full sleep cycles. The calculated AHI was the AHI with optimal therapeutic settings.

## Statistical analysis

Statistical analysis was performed using SPSS (version 24, SPSS Inc, Chicago, IL). Quantitative data are reported as mean and standard deviation (SD) or as median and Q1-Q3 when not normally distributed. Qualitative variables are reported as frequencies and percentages. The Shapiro-Wilk Test was used to determine whether

the continuous variables were normally distributed. When the Statistic *W* was  $> 0.90$  the data was considered normally distributed. Baseline characteristics and PSG parameters were analyzed by using descriptive statistics. A *p*-value of  $< 0.05$  was considered to prove statistical significance.

## RESULTS

### *Baseline characteristics*

Twenty-three patients receiving UAS implantation were included. In total, four patients were excluded due to technical problems during the daytime PSG. Two patients had technical interruptions because of software failure, therefore it was not possible to register sufficient continuous sleep. The other two patients had connection problems with the implanted pulse generator (IPG) and therefore awakened frequently, giving unreliable results. Excluded patients are shown in appendix 1.

**Table 1.** Patient characteristics

	<b>Total</b>
<b>Number of patients (N)</b>	19
<b>Sex (male: female)</b>	16:3
<b>Age (years)</b>	57.0 $\pm$ 11.0
<b>BMI (kg/m<sup>2</sup>)</b>	27.2 $\pm$ 2.4
<b>Pre-operative AHI (events/hr)</b>	41.2 $\pm$ 10.8
<b>Time from activation device to titration (months)</b>	6 [4; 9]
<b>Device usage (hrs/week)</b>	48.0 [42.0; 54.0]

Data presented as mean  $\pm$  standard deviation or median [Q1, Q3]

*BMI* body mass index, *AHI* apnea-hypopnea index

In total, 19 patients were included for statistical analysis. Thus far, fourteen completed their 12-months follow-up overnight PSG. The majority of the patients was male (84%), at the time of titration the mean age was  $57 \pm 11$  years with a mean BMI of  $27.2 \pm 2.4$  kg/m<sup>2</sup>. Based on baseline PSG data, the mean pre-operative AHI was  $41.2 \pm 10.8$  events per hour. The baseline patient characteristics are shown in **table 1**. The median time between device activation and titration was 6 months and the median device usage was 48 [42.0; 54.0] hours a week before titration.

### Effect on sleep architecture

A comparison of daytime PSG to overnight PSG sleep architecture is shown in **table 2**. Patients slept  $3.4 \pm 1.0$  hours during the daytime PSG, this was significantly shorter than during overnight PSG  $6.8 \pm 1.0$  hours ( $p < 0.001$ ). Sleep efficiency was comparable 80.3% [65.7; 90.4] during daytime and 85.2% [84.0; 90.8] during overnight PSG ( $p = 0.177$ ). Sleep latency was significantly shorter during the daytime PSG 3.0 [1.1; 10.0] minutes than during overnight PSG 7.6 [5.8; 17.0] minutes. No significant differences were found regarding sleep stages N2 and N3 ( $p = 0.107$ ,  $p = 0.103$ ). During the daytime PSG significantly more N1 sleep was found 7.8 [6.1; 13.2] % of TST than during the overnight PSG 4.5 [2.2; 5.0] % of TST ( $p = 0.003$ ). Significantly less REM sleep occurred during the daytime PSG  $12.9 \pm 8.1\%$  of TST than during overnight PSG  $24.7 \pm 7.7\%$  of TST ( $p = 0.007$ ). Two patients did not have any REM sleep during the daytime PSG. The median amount of sleep cycles during the daytime PSG was three complete cycles compared to the overnight PSG with a median of four complete cycles.

**Table 2.** Polysomnography outcomes titration daytime PSG versus follow-up overnight PSG

	Total (n=19) DPSG	Total (n=14) FU-NPSG	p-value
<b>TST (hour)</b>	$3.4 \pm 1.0$	$6.8 \pm 1.0$	$<0.001^*$
<b>Sleep efficiency† (%)</b>	80.3 [65.7; 90.4]	85.2 [84.0; 90.8]	0.177
<b>Sleep latency (minutes)</b>	3.0 [1.1; 10.0]	7.6 [5.8; 17.0]	0.016*
<b>REM latency (minutes)</b>	69.0 [59.0; 121,8]	80.8 [64.8; 132.5]	0.551
<b>Sleep stage N1 (% of TST)</b>	7.8 [6.1; 13.2]	4.5 [2.2; 5.0]	0.003*
<b>Sleep stage N2 (% of TST)</b>	$53.9 \pm 10.4$	$43.1 \pm 11.5$	0.107
<b>Sleep stage N3 (% of TST)</b>	$22.2 \pm 8,1$	$27.9 \pm 8.7$	0.103
<b>Sleep stage REM (% of TST)</b>	$12.9 \pm 8.1$	$24.7 \pm 7.7$	0.007*
<b>Sleep cycles</b>	3 [2; 3]	4 [4; 5]	0.005*
<b>REM periods</b>	2 [1; 3]	4 [3; 4]	0.003*

Data presented as mean  $\pm$  standard deviation or median [Q1, Q3]

\* p value  $<0.05$  comparing titration daytime PSG with follow-up overnight PSG

† Sleep efficiency = TST / time in bed  $\times 100\%$

DPSG daytime polysomnography, FU-NPSG follow-up overnight polysomnography, TST total sleep time, REM rapid eye movement, NREM non-rapid eye movement

*Success and practicality daytime titration*

The outcomes of the (pre-) daytime titration in terms of feasibility are shown in **table 3**. The majority of patients was able to stay awake after midnight until the start of the daytime PSG. In total, two patients slept after midnight with a maximum of 150 minutes. Eighty-four percent of the patients was able to sleep 30 minutes in the final UAS device settings. Device polarity settings or amplitude voltage were changed in 47.4% of the patients following the titration. The exact changes in setting and stimulation amplitude in voltage for every patient are presented in Appendix 2.

**Table 3.** Outcome (pre-) daytime titration

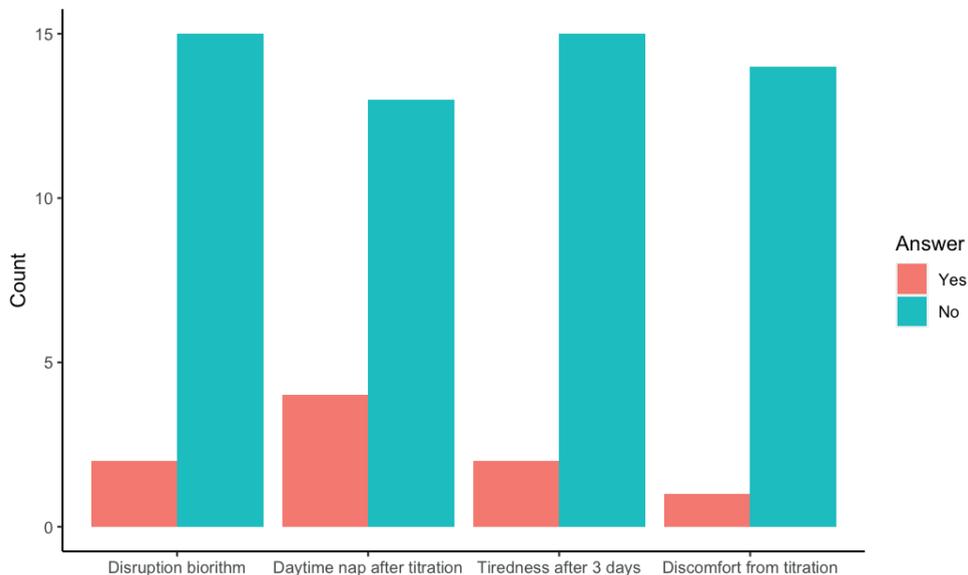
Pre-titration	N (total = 19)	Outcomes
Time slept before midnight (00:00) before titration (minutes)	16	71 ± 59
Time slept after midnight (00:00) before titration (minutes)	17	0 [0; 0] (0-150)
Participants consuming caffeine after midnight	17	3 (21.4%)
Participants consuming alcohol day before titration	17	1 (6.3%)
Participants consuming nicotine after midnight	17	2 (13.3%)
Titration		
Slept 30 minutes in final settings	19	16 (84.2%)
Observed NREM in supine position in final settings	19	12 (63.2%)
Observed REM in supine position in final settings	19	6 (31.6%)
Setting and voltage not changed after titration*	19	10 (52.6%)
Voltage changed after titration*	19	3 (15.8%)
Setting and voltage changed after titration*	19	6 (31.6%)

Data presented as mean ± standard deviation or median [Q1, Q3] with range or numbers and percentages in parenthesis.

\*Appendix shows changes in settings and voltages. NREM non-rapid eye movement, REM rapid eye movement

*Subjective patient experience*

Almost all patients (94.1%) had a positive experience with the daytime titration; one patient experienced discomfort from the titration. (**Fig. 1**) The majority of patients (88.2%) did not suffer from tiredness three days after titration and could pick up their normal sleeping habits without any problems. Four patients (23.5%) took a daytime nap the day after titration.

**Figure 1.** Subjective patient experience with daytime titration (n=17)

### *Titration and follow-up outcome*

The median AHI decreased significantly ( $p=0.001$ ) from baseline with 40.4 [34.6; 46.9] events per hour to 9.0 [3.3; 17.0] events per hour during titration. At 12-months follow-up the AHI was 12.2 [6.7; 24.9] events per hour, not significantly different from the titration AHI ( $p=0.158$ ). There was also a statistically significant reduction of AI, RDI, ODI, arousal index, lowest saturation and time slept with  $SpO_2 < 90\%$ , as shown in **table 4**. The ODI (3% and 4%) during titration was not significantly different from the follow-up ODI (respectively  $p=0.272$  and  $p=0.875$ ). Time slept in supine position did not differ significantly between baseline, titration and follow-up.

**Table 4.** Results UAS therapy from baseline PSG, daytime titration PSG and follow-up PSG

	Baseline PSG		Daytime titration PSG		Follow-up PSG 12 months		p-value
	N (total=19)	Outcome	N (total=19)	Outcome	N† (total=14)	Outcome	
Total AI (events/hr)	19	17.8 [10.1; 29.3]	19	2.0 [0.0; 5.4]	14	4.1 [0.5; 13.0]	0.002*
Total AHI (events/hr)	19	40.4 [34.6; 46.9]	19	9.0 [3.3; 17.0]	14	12.2 [6.7; 24.9]	0.001*
Supine AHI (events/hr)	18	55.8 [35.5; 74.9]	14	7.9 [2.1; 33.7]	14	21.9 [9.3; 48.6]	0.011*
Non-supine AHI (events/hr)	18	29.5 [19.4; 40.6]	17	5.1 [1.2; 10.8]	14	4.4 [0.5; 20.6]	0.006*
AHI REM (events/hr)	19	34.3 [19.6; 48.8]	15	10.4 [1.6; 28.8]	14	19.3 [1.8; 25.8]	0.001*
RDI (events/hr)	19	42.1 [35.3; 46.9]	19	9.0 [5.6; 20.4]	14	12.6 [7.1; 26.5]	0.001*
Arousal index (events/hr)	19	21.4 [16.4; 37.2]	19	12.9 [6.0; 19.0]	14	11.6 [6.7; 19.2]	<0.001*
% of TST in supine position	19	35.5 [14.6; 52.2]	19	51.9 [0.0; 69.6]	14	38.7 [5.5; 61.5]	0.872
ODI (3%, events/hr)	19	43.4 [29.2; 51.3]	18	18.5 [10.5; 31.1]	12	20.6 [12.1; 24.1]	0.003*
ODI (4%, events/hr)	11	37.7 [27.4; 44.7]	18	12.6 [6.0; 20.9]	12	10.4 [8.7; 16.7]	0.009*
Mean saturation (%)	19	94.0 [93.0; 95.0]	19	94.0 [94.0; 95.0]	12	93.0 [92.3; 94.0]	0.098
Lowest saturation (%)	19	83.8 ± 4.7	19	89.0 ± 2.7	12	86.3 ± 2.4	<0.001*
Time SpO <sub>2</sub> <90% (minutes)	19	9.2 [0.5; 32.9]	19	0.0 [0.0; 0.7]	12	3.6 [0.5; 17.0]	<0.001*
BMI (kg/m <sup>2</sup> )	19	27.2 ± 2.4	19	28.0 ± 2.8	14	27.6 ± 2.6	0.002*

Data presented as mean ± standard deviation or median [Q1, Q3], \* p value <0.05

† n=14 because 5 patients did not yet complete the follow-up overnight PSG

α comparing baseline overnight PSG with titration daytime PSG

β comparing titration daytime PSG with follow-up overnight PSG

NPSG overnight polysomnography, DPSG daytime polysomnography, FU-NPSG follow-up polysomnography, AI apnea-index, AHI apnea-hypopnea index, REM rapid eye movement, RDI respiratory disturbance index, TST total sleep time, ODI oxygen desaturation index, SpO<sub>2</sub> peripheral capillary oxygen saturation.



## DISCUSSION

This single-center prospective study is the first study to demonstrate that a daytime PSG to perform titration is a feasible alternative for a conventional overnight titration for OSA patients with UAS therapy. Even though patients slept significantly shorter during the daytime PSG, this was enough time to complete the titration successfully with 30 minutes sleep in final therapeutic settings in 84.2% of the patients. Furthermore, 94.1% of the patients had a positive experience with the daytime titration and did not experience any discomfort. Respiratory OSA outcomes were significantly reduced during titration and were maintained at the 12-months follow-up.

To the best of our knowledge, no other study has investigated the role of daytime PSG for titration of UAS. A few studies have already proven that daytime PSG is an appropriate procedure for titration of CPAP. [8, 11, 12, 14, 16] The American Academy of Sleep Medicine (AASM) clinical practice guideline states that a CPAP titration should be carried out for at least three hours during NREM and REM sleep in supine position. [17] This is comparable to our study where patients averagely slept  $3.4 \pm 1.0$  hours while all sleep stages were observed including REM in supine position in final settings in 31.6% of the patients.

To ensure patients were able to sleep during the daytime PSG they were asked to stay awake the night before the titration. A concern might be that overnight sleep deprivation in OSA patients alters sleep architecture and AHI results. For example, Persson and Svanborg observed an increase of AHI in OSA patients after sleep deprivation, suggesting that daytime studies are not suitable to determine the severity of OSA. [18] In our study however, the daytime PSG was used to titrate the UAS therapy. Our results show that there are no significant differences between the AHI at the 12-months follow-up 12.0 [6.7; 24.9] and the titration AHI 9.0 [3.3; 17.0] ( $p=0.158$ ). This means that the optimal settings found during titration were effective even with a possible altered AHI at the time of titration. On the other hand, a significantly shorter period of REM sleep was found during the daytime PSG  $12.9 \pm 8.1$  compared to  $24.7 \pm 7.7$  overnight PSG (% of TST) ( $p=0.007$ ). Since it is known that during REM sleep oxygen desaturation is more severe than during NREM sleep in patients with OSA, this could have underestimated the OSA severity during titration. [19] Again our results at 12-months follow-up showed no significant difference and therefore this argument had no influence on our titration. Also, the supine body position often increases the severity of apneas during therapy. Our

study did not correct for the effect of body position during the daytime PSG. However no significant differences were found for % TST in supine position between baseline, titration and follow-up PSG.

This study is not without limitations. Yearly approximately 35 patients with OSA are recruited for UAS therapy in the OLVG hospital and we were able to include 23 patients in this study. [15] The small sample size and the 5 patients who did not yet complete their 12-months follow-up should be taken into consideration when interpreting the results. Some differences might be significant when larger studies are performed. Ideally, we would have compared the daytime titration PSG to an overnight titration PSG. Unfortunately, this was not feasible during this pilot study. Due to the fact that during the pre-op PSG, patients are suffering from untreated OSA, we opted to compare both sleep architecture and respiratory outcomes with the 12 months follow-up PSG. Furthermore, we did not prohibit patients to consume caffeine the night before the daytime PSG. This might have influenced the sleep architecture but due to the group size (3 patients who consumed caffeine) we were not able to prove significant differences.

Our experience with activation and titration has developed over the past few years. We know now it pays off to be flexible and to take more time to adjust and find a therapeutic but comfortable setting for patients. Whenever patients report subjective improvements during the first few months, this implies good therapy response. The titration could then be postponed or in the future even be replaced by a PSG at home to confirm therapy response. In this study device settings changed based on titration outcomes in 47.4% of the patients, suggesting that in all other cases the optimal settings were already found previously. Potentially this would obviate the need for titration in certain patients. A recent study by Steffen et al. assessed the use of home sleep tests for the treatment-adjustment phase of UAS. They concluded that home sleep tests had clinical advantages and were useful as a second-line titration control method under several conditions. [20] In addition, in a recently published case study, Huyett and Stagnone described the use of pulse oximetry as an addition to home titration for UAS therapy optimization before actual in-lab titration. They also concluded that certain patients could possibly directly proceed to a home sleep test instead of in-lab PSG titration. [21]

When comparing sleep architecture, sleep efficiency was similar for the daytime PSG compared to the overnight follow-up PSG ( $p=0.177$ ). These results are

comparable with Miyata et al. who also found no significant difference for sleep efficiency when comparing a daytime PSG with an overnight PSG for diagnosing OSA. [10] Sleep latency was significantly shorter during the daytime PSG, with 3.0 [1.1; 10.0] minutes compared to 7.6 [5.8; 17.0] minutes overnight. The overnight sleep latency is comparable with a normal sleep latency for healthy people between 50-64 years. [22] Sleep deprivation the night before titration might explain the shorter sleep latency during the daytime PSG. [23] No significant difference was found for N2 and N3 sleep during the daytime PSG compared to the follow-up overnight PSG. The amount of N2 and N3 sleep found in this study is similar to the study of Boulos et al. who investigated sleep architecture in healthy people between 50-64 years. The independent effect of OSA on sleep architecture remains unclear. Shahveisi et al. found that OSA independently has the tendency to increase N1 sleep. [24] This perhaps could explain the significant difference we found in the amount of N1 sleep during the daytime PSG 7.8 [6.1; 13.2] % of TST compared to the overnight PSG 4.5 [2.2; 5.0] % of TST ( $p=0.003$ ). Titration was performed during the daytime PSG meaning that therapy was not consistent resulting in occasional OSA compared to the follow-up overnight PSG where therapy was used the entire night.

We found similar results regarding respiratory outcomes with UAS therapy during titration and 12-months follow-up compared to similar larger studies. First, the results of the recently published ADHERE study show a median AHI reduction from 32.8 [23.6; 45.0] events per hour at baseline to 9.5 [4.0; 18.5] events per hour after 12 months. [25] These are similar to our results; a reduction in AHI from 40.4 [34.6; 46.9] events per hour at baseline to 12.2 [6.7; 24.9] events per hour after 12 months. In the original STAR trial, the AHI decreased from 28.2 events per hour at baseline to 8.7 events per hour at 12 months. [26] Furthermore, device usage in our study (48 [42; 54] hours per week) was comparable to a similar study (47.0 [38.5; 52.0] hours per week after six months). [20]

The growing amount of patients using UAS therapy asks for a more accessible way to perform titrations. Performing these titrations during the night makes it very labour-intensive and expensive. The technician is subsequently not available for the day shift and many sleep technicians dislike night shifts because of understandable personal circumstances. The benefit of a daytime PSG is that more titrations can be performed and sleep technicians do not have to work during the night. The implications of performing daytime PSG for titration include being able to perform more titrations with shorter

waiting time and less labor-intensive work for sleep technicians. Patients experienced this daytime study as positive and were willing to repeat it in the future if necessary.

## CONCLUSION

Daytime titrations are a valuable alternative for conventional overnight titrations. Our findings suggest the implementation of daytime titrations as standard of care. This will contribute to easier logistics and better work circumstances for sleep technicians without jeopardizing titration quality.

## Appendix

### Appendix 1. Excluded patients for analysis (n=4)

Record number	Reason exclusion
110001	Technical interruptions, not able to register 30 minutes of continuous sleep.
110002	Technical interruptions, software failure (update and flatline signals). No setting found for functional therapy.
110007	Connection problems IPG, therefore continual repositioning and no entire sleep cycle registered.
110021	Connection problems IPG, therefore frequent awakenings and no NREM 3 and REM sleep.

*IPG* Implantable pulse generator, *REM* rapid eye movement, *NREM* non rapid eye movement

**Appendix 2.** UAS device polarity setting and amplitude outcome

<b>Patient (n=19)</b>	<b>Setting pre-titration Amplitude in V</b>	<b>Setting after titration Amplitude in V</b>	<b>Amplitude changed? (yes/no)</b>
<b>1</b>	2.3 Unipolar (0 - 0)	2.3 Unipolar (0 - 0)	No
<b>2</b>	2.1 Bipolar (+ - +)	1.6 Unipolar (0 - 0)	Yes *
<b>3</b>	1.3 Bipolar (+ - +)	1.1 Bipolar (+ - +)	Yes
<b>4</b>	2.3 Bipolar (+ - +)	2.5 Bipolar (+ - +)	Yes
<b>5</b>	0.8 Bipolar (+ - +)	1.3 Bipolar (+ - +)	Yes
<b>6</b>	1.2 Unipolar (0 - 0)	2.6 Bipolar (+ - +)	Yes *
<b>7</b>	1.1 Unipolar (0 - 0)	1.8 Bipolar (+ - +)	Yes *
<b>8</b>	2.1 Bipolar (+ - +)	2.1 Bipolar (+ - +)	No
<b>9</b>	2.3 Bipolar (+ - +)	2.3 Bipolar (+ - +)	No
<b>10</b>	0.9 Bipolar (+ - +)	0.9 Bipolar (+ - +)	No
<b>11</b>	1.7 Bipolar (+ - +)	1.7 Bipolar (+ - +)	No
<b>12</b>	1.7 Bipolar (+ - +)	0.9 Unipolar (0 - 0)	Yes *
<b>13</b>	2.1 Unipolar (- 0 -)	4.4 Bipolar (+ - +)	Yes *
<b>14</b>	2.6 Bipolar (+ - +)	2.6 Bipolar (+ - +)	No
<b>15</b>	3.9 Bipolar (+ - +)	3.9 Bipolar (+ - +)	No
<b>16</b>	3.1 Bipolar (+ - +)	3.1 Bipolar (+ - +)	No
<b>17</b>	1.0 Bipolar (+ - +)	1.0 Bipolar (+ - +)	No
<b>18</b>	1.2 Bipolar (+ - +)	0.7 Unipolar (0 - 0)	Yes *
<b>19</b>	2.4 Bipolar (+ - +)	2.4 Bipolar (+ - +)	No

\* polarity setting also changed

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